Oral Presentations

ALLOGENEIC TRANSPLANTS

7

THE INCIDENCE AND NATURAL HISTORY OF PURE RED CELL APLASIA IN MAJOR ABO MISMATCHED HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS RECEIVING MODERN REDUCE INTENSITY AND REDUCED TOXICITY REGIMENS

Aung, F.M.[1], Lichtiger, B.[1], Alousi, A.[2], Hosing, C.[2], Qazilbash, M.[2], de Lima, M.[2], Kebriaei, P.[2], Khouri, I.[2], Champlin, R.C.[2], Popat, U.[2]
[1] University of Texas MD Anderson Cancer Center, Houston, TX;
[2] University of Texas MD Anderson Cancer Center, Houston, TX

Background: Major ABO matching in Hematopoietic stem cell transplantation (HSCT) is not considered a contraindication to Allogeneic HSCT transplantation. Modern reduced intensity conditioning regimens, and reduced toxicity regimens like busulfan and fludarabine cause much less myeloablation than conventional myeloablative regimens like cyclophosphamide with busulfan or TBI. Therefore recipient cells producing donor red cell specific antibody are more likely to survive after a major ABO mismatched transplant and cause red cell aplasia. We hypothesized that there is an increased incidence of PRCA in Allogeneic HSCT patients who receive reduced intensity and reduced toxicity conditioning for stem cell transplantation. The purpose of this study is to estimate the incidence and describe the natural history of PRCA after HSCT.

Patients and Methods: All Major ABO mismatched Allogeneic Hematopoietic stem cell transplants during a 2-year period (2007-2008) were prospectively analyzed. PRCA was defined as lack of erythroid precursors on bone marrow examination 30 days post-transplant, lack of appearance of donor cells on Forward red cell Typing and being RBC transfusion dependent.

Results: Between 2007 and 2008, 596 patients underwent reduce intensity Allogeneic HSCT transplants. The Hematopoietic stem cells were Major ABO incompatible in 155(26%). Twelve (7.7%) patients fulfilled the criteria for PRCA with 6 males/ 6 females and a median age 51 years (range 24-73). The diagnoses were as follows: AML/MDS (8), CML/MPD (2), ALL (1), Myeloma (1). The conditioning regimen was [Fludarabine/Busulfan/ATG (9), Fludarabine/Bulsulfan (3), Fludarabine/Melphalan (2) and Fludarabine/Melphalan/ATG (1). At day 30 chimerism studies showed a median of 90% donor hemopoiesis in T lineage (range 21-100%)and a median of 100% (range 99-100%) in myeloid lineage Recovery of erythropoiesis was noted in 10 patient with a median of 257 days (range 87-364) after transplant. Four (33%) patients died (1 from disease recurrence and 3 from transplant related mortality). Two of the patient who died did not achieve red cell recovery. All the patients had significant rbc transfusion requirement and developed iron overload with significant elevation of transaminases due to iron deposition in liver.

Conclusion: PRCA frequently (7.7%) occurs with current conditioning regimens necessitating red cell transfusions for many months after transplant resulting in significant iron overload.

Table 1. Pre-and Post Transplant Data

	Pre-Transplant	Post-Transplant	
	Median (Range)	Median (Range)	Normal Range
Serum Total Bilirubin	0.5 (0.2-1.3)	0.7 (0.1-1.0)	0.0-1.0 mg/dl
Lactate Dehydrogenase	471 (212-2145)	1007 (349-1431)	313-618 IU/L
Alkaline Phosphatase	55 (36-140)	84 (69-238)	38-126 IU/L
Alanine Aminotransferase	15 (11-54)	26 (12-305)	7-56 IU/L
Hemoglobin	8.4 (7.9-13.7)	11.3 (6.6-13.9)	14.0-18.0 g/dl
Serum Ferritin	1172 (81-3307)	4134 (1437-11634)*	22-322 ng/ml
Liver iron Concentration for 6/8 surviving PRCA patients		15.8 mcg of iron (12.5- 25 mcg/dry liver weight)	
RBCs Transfused		Av 41 (15-131 units)	
RBCs Transfusion Dependence		265 (97-439 days)	
Median Follow-up		22 (3-44 months)	

*Post-transplant serum ferritin was not obtained on 1 patient

8

INCREASING THE DOSE OF BUSULFAN RESULTS IN LOWER RELAPSE RATES AND HIGHER NON-RELAPSE MORTALITY IN PATIENTS WITH MDS/AML UNDERGOING REDUCED INTENSITY ALLOGENEIC STEM CELL TRANSPLANTATION

Chen, Y.-B.[1], Sun, L.[3], Kim, H.[3], Alyea, E.P.[2], Armand, P.[2], Attar, E.C.[1], Ballen, K.K.[1], Cutler, C.[2], Dey, B.R.[1], Koreth, J.[2], McAfee, S.L.[1], Spitzer, T.R.[1], Antin, J.H.[2], Soiffer, R.J.[2], Ho, V.T.[2]
[1] Massachusetts General Hospital, Boston, MA; [2] Dana-Farber Cancer Institute, Boston, MA; [3] Dana-Farber Cancer Institute, Boston, MA

Reduced intensity conditioning (RIC) regimens have allowed many patients who would not have tolerated myeloablative conditioning (MAC) to undergo allogeneic hematopoietic stem cell transplantation (HSCT). Even so, dose intensity in RIC regimens vary and may affect treatment outcomes. In this analysis, we asked if a difference in intravenous busulfan dosing (3.2 mg/kg vs. 6.4 mg/kg) in a fludarabine/busulfan (Flu/Bu) RIC regimen would affect HSCT outcomes. A total of 188 patients with MDS or AML underwent Flu/Bu RIC HSCT from matched related (MRD) or matched unrelated donors (MUD) at two partner institutions between 2004 and 2008. 118 patients received Bu1 (busulfan 0.8 mg/kg/d × 4 with daily fludarabine) while 70 patients received Bu2 (busulfan 1.6 mg/kg/d in divided doses daily × 4 with daily fludarabine). Patients had similar clinical characteristics, including disease risk status, except that patients receiving Bu1 were younger (median age 58 vs 62, $p = .0006$), received more sirolimus based GVHD prophylaxis regimens (88% vs 26%, $p < .0001$), and had longer follow-up (median, Bu1 39.1 months vs Bu2 18.3 months, $p < .0001$). The choice of RIC regimens was based on institutional standard, enrollment on specific protocols, and physician preference. The incidence of grades II-IV acute GVHD (Bu1 19% vs Bu2 17%, $p = 0.82$) and chronic GVHD (2-year cumulative incidence, Bu1 42% vs Bu2 32%, $p = .07$) were similar. Patients who received Bu1 had lower rates of non-relapse mortality (NRM) at 1-year (Bu1 2% vs Bu2 9%) and 2-years (Bu1 4% vs Bu2 11%, $p = 0.013$). Cumulative rates of relapse at 1-year (Bu1 59% vs Bu2 49%) and 2-years (Bu1 68% vs Bu2 49%, $p = .022$) were significantly higher in patients receiving Bu1.

Table 1. Cumulative Incidences of NRM and Relapse

	Bu1	Bu2	p-value
1-year NRM	1.7%	8.6%	
2-year NRM	3.7%	11.1%	0.013
1-year Relapse	59.3%	48.6%	
2-year Relapse	68.1%	48.6%	0.022

Progression-free survival at 1-year (Bu1 39% vs Bu2 43%) and 2-years (Bu1 28% vs Bu2 40%, $p = .20$) was similar between the two groups. Overall survival at 1-year (Bu1 52% vs Bu2 61%) and 2-years (Bu1 39% vs Bu2 50%, $p = .22$) was also similar. In patients with MDS/AML undergoing Flu/Bu RIC SCT, Bu2 appears to have significantly lower rates of disease relapse, yet higher rates of NRM. Longer follow-up is needed to confirm if these differences are durable and if there are specific risk groups which would benefit more from the increased intensity of RIC.